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# Survival Benefits of Heart and Lung Transplantation

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## Objective

Heart and lung transplantation has gained acceptance as therapy for end-stage cardiac and pulmonary failure. The early and intermediate survival benefits of one center's 10-year experience with 177 patients undergoing thoracic transplantation were examined.

## Summary Background Data

As experience in cardiac and pulmonary transplantation has increased, improvements in patient selection, organ preservation, preoperative support, and perioperative care have significantly reduced the early threats to patient survival. Graft dysfunction due to chronic rejection appears to be the main risk for longer-term survival, and data compiled by the United Network for Organ Sharing (UNOS) indicate a 70% 5-year survival for heart transplants and a 50% 5-year survival for lung transplant recipients.

## Methods

The medical records of 120 heart recipients, 52 lung transplant recipients, and 5 heart–lung recipients were reviewed. Cumulative survival estimates were made using Kaplan-Meier analysis. The etiologies of operative and long-term mortality in each transplant population were identified. A comparison of long-term survival after heart transplantation *versus* coronary revascularization in a group of patients with ischemic cardiomyopathy was performed.

## Results

Operative mortality in both the cardiac and pulmonary transplant recipients was 8%. From 1990 to 1995, 70 consecutive adult cardiac transplant procedures were performed without an operative mortality. Three of five patients survived heart–lung transplantation. The extended actuarial survival rate at 5 years was 80% for the cardiac transplant recipients. The 2-year actuarial survival rate for the lung transplant recipients was 88%. Graft dysfunction was the most common cause of operative mortality in the heart transplant group whereas infection was responsible for most of the operative mortality after lung transplantation.

## Conclusions

Cardiac and pulmonary transplantation can be applied to morbidly ill patients with excellent operative and intermediate-term survival.

Since the clinical introduction of heart, lung, and heart–lung transplantation in the 1960s, thoracic transplantation has become an established form of therapy for patients with end-stage heart and lung disease. Current United Network for Organ Sharing (UNOS) statistics indicate that the annual number of thoracic organ replacements is approximately 2000 hearts per year, 800 lungs per year, and 60 heart–lungs per year. The transplant survival data compiled by UNOS indicate a 70% 5-year survival rate in heart transplant recipients and a 50% 5-year survival rate in lung transplant recipients. The greatest impediment to increased application of transplantation for end-stage heart and lung disease has been a limitation of donors. This has resulted in large waiting lists (3000 hearts, 1600 lungs) and has led to the development of alternative and currently experimental interventions that might enhance survival in these end-stage patients. These new technologies include laser created transmyocardial vascular channels, cardiomyoplasty, and permanent implantation of left ventricular assist devices for cardiac patients,[1] and volume reduction lung surgery for patients with advanced chronic obstructive pulmonary disease. The benefits of such new therapies for end-stage heart and lung disease are yet to be defined and compared with the realities of heart and lung transplantation. The purpose of this report is to review one center's experience in thoracic transplantation in the current cyclosporine era and to document the survival benefits that can be achieved with heart, lung, and heart–lung transplantation.

## MATERIALS AND METHODS

The records of 177 patients receiving thoracic organ replacement at Duke University Medical Center between April 1985 and April 1995 were reviewed. The cardiac transplant program was initiated in 1985, and the lung transplant and heart–lung transplant programs began in 1992 (Fig. 1). All transplant operations performed since 1987 were performed by the same group of transplant surgeons, and an attending surgeon participated in all donor procurement procedures.

### Patient Selection Criteria for Transplantation

The general indications followed for cardiac transplantation included age younger than 65 years with class III to IV symptoms of congestive heart failure associated with an ejection fraction of less than 20%.[2] These patients were considered only if pulmonary vascular resistance measured less than 7 wood units because of the high risk of donor right ventricular failure in recipients with pulmonary hypertension.[3] Other criteria included absence of irreversible renal or hepatic dysfunction, absence of infection, and demonstrated compliance with medical therapy.

The indications for lung transplantation included the presence of end-stage lung disease with a life expectancy less than 18 months. Generally, the forced expiratory volume in 1 second ($FEV_1$) was less than 20% predicted for patients with chronic obstructive pulmonary disease and less than 30% predicted for patients with cystic fibrosis.[4] Pulmonary transplantation was applied to patients with primary and secondary pulmonary hypertension when the mean pulmonary artery pressure was greater than 85 mmHg and the patient had class III or greater symptoms of respiratory insufficiency. Single-lung transplantation was applied to patients younger than 65 years of age without infectious lung disease, whereas bilateral sequential lung transplantation was applied to patients younger than 55 years of age, those with infectious lung disease (cystic fibrosis), and patients with either primary or secondary pulmonary hypertension who had normal left ventricular function. Patients accepted for lung transplantation had no other significant systemic disease, were nonsmokers, and had demonstrated medical compliance. Heart–lung transplantation was reserved for patients with Eisengmenger's syndrome with *biventricular* failure or complex congenital heart disease not correctable with conventional cardiac surgery.

### Operative Techniques

The operative techniques of heart, lung, and heart–lung implantation as well as donor harvest and preservation were standardized according to institutional protocols. All hearts were preserved with a routine crystalloid hyperkalemic cardioplegia, and lungs were flushed with a modified Euro-Collins solution preceded by 500 $\mu$g of prostaglandin $E_1$. Aprotinin was used routinely for heart transplant procedures performed through a prior sternotomy and all lung transplants requiring cardiopulmonary bypass. Inhaled nitric oxide has been used in the past 12 months for heart transplant recipients with significant right ventricular dysfunction and almost routinely after single or bilateral lung transplantation. A standard cyclosporine-based triple drug immunosuppressive regimen was used for all transplant recipients.[5]

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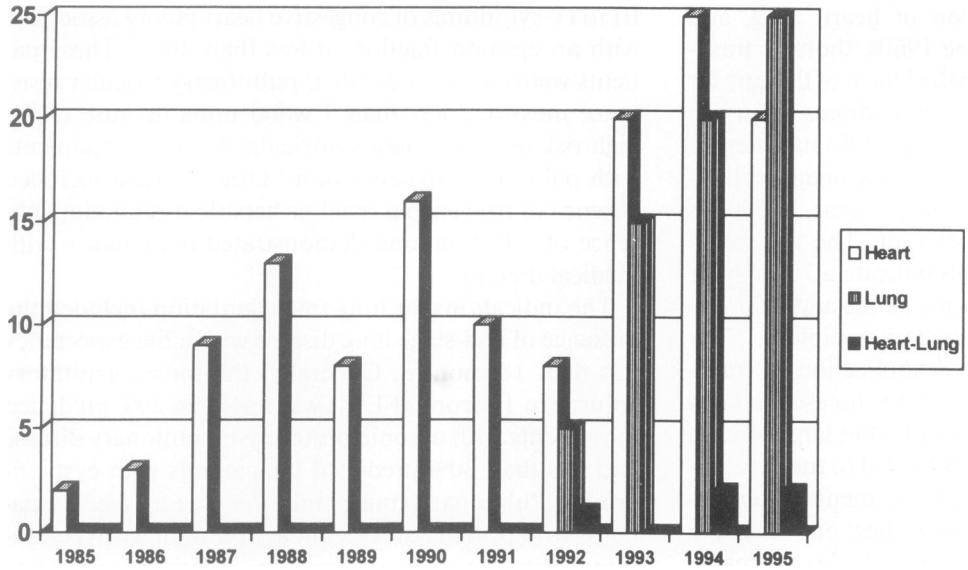


**Figure 1.** Thoracic organ transplant volume per year at Duke University Medical Center.

## Patient Characteristics: Heart Transplantation

The cardiac transplant group included 120 patients, with 86 males and 34 females (Table 1). The mean age at the time of transplantation was 45.6 ± 3.6 years, with an age range of 3 weeks to 64 years. The most common diagnosis of the recipient was ischemic cardiomyopathy (n = 60), with idiopathic cardiomyopathy representing the other major recipient diagnosis (n = 51). The remainder of the recipient diagnoses are listed in Table 2.

The mean pretransplant ejection fraction was 15% ± 5% with a range of 4% to 21%. Of the 120 heart recipients, 16 experienced an episode of cardiac arrest requiring cardiopulmonary resuscitation (CPR) preoperatively. The severity of illness of this patient population is reflected by the fact that 104 patients were UNOS Status 1 before transplantation (requiring mechanical or inotropic drug support in intensive care) and the remainder were UNOS Status 2. Approximately one third of the patients had undergone previous sternotomy for coronary artery bypass grafting or other cardiac procedures. A mechanical bridge to transplantation was used in 31 patients when inotropic support was inadequate (Table 3). An intra-aortic balloon pump was used for circulatory support in 25 patients, predominantly those with ischemic cardiomyopathy, for periods of up to 160 days. When an intra-aortic balloon pump was inadequate to provide hemodynamic stability, the HeartMate left ventricular assist device (Thermo Cardiosystems, Inc., Woburn, MA) was used to support 4 patients (range, 20–105 days) who were all successfully transplanted. One early patient was supported with the Anstadt cup ventricular actuator (Advanced Resuscitation Innovations, Inc., Tipp City, OH) for 3 days before being successfully transplanted.[6] The average pretransplant length of stay for Status 1 patients was 54 ± 7 days.

Cardiac donor selection criteria included age younger than 60 years with a negative history of cardiac disease. A two-dimensional echocardiogram was performed on virtually all potential donors, and significant wall motion abnormalities usually would disqualify a heart for transplantation.[7] Acceptable donor inotropic support was defined as 15 μg/kg per minute (or less) of dopamine and coronary arteriograms were performed, when possible, on donors older than 50 years of age. Significant coronary lesions (≥ 50% stenosis) would preclude use of a donor heart.[8]

**Table 1. THORACIC TRANSPLANT RECIPIENTS: CLINICAL CHARACTERISTICS**

| Organ | No. of Patients | Male/Female | Age (yr) (range) |
|---|---|---|---|
| Heart | 120 | 86/34 | 46.5 (3 wk–64 yr) |
| Lung | 52* | 29/33 | 46.5 (20–66 yr) |
| Heart–lung | 5 | 3/2 | 33.8 (17–42 yr) |

* Single, 30 patients; bilateral, 22 patients.

## Patient Characteristics: Lung Transplantation

Between 1992 and April 1995, 52 patients underwent lung transplantation. The group included 29 men and 23 women, with a mean age of 46.5 ± 3.5 years (range, 20–66 years). Single-lung transplantation was performed in

**Table 2. HEART TRANSPLANT RECIPIENT DIAGNOSIS (N = 120)**

| Diagnosis | No. |
|---|---|
| Ischemic cardiomyopathy | 60 |
| Idiopathic cardiomyopathy | 51 |
| Congenital | 4 |
| Restrictive | 2 |
| Postpartum | 2 |
| Viral myocarditis | 1 |

30 patients; 22 patients received bilateral sequential lung transplants. The most common recipient diagnosis was chronic obstructive pulmonary disease (24 patients), with cystic fibrosis representing the next largest group (10 patients), as summarized in Table 4. Bilateral lung transplantation was performed on all patients with cystic fibrosis, primary pulmonary hypertension, and Eisenmenger's syndrome with intact left ventricular function.[9] Bilateral sequential lung transplants also were performed on selected young patients (less than 50 years) with obstructive or restrictive disease to provide them with the potential for a greater long-term survival, anticipating that the risk for chronic graft dysfunction secondary to bronchiolitis obliterans would be less severe.[10]

Of the 52 patients undergoing lung transplantation, 13 patients were critically ill requiring pretransplant hospitalization. Ventilator support was required for five patients for a period of 8 days to 4 months. Of the patients requiring pretransplant mechanical ventilation, four of five survived transplantation; one patient with cystic fibrosis died of *Pseudomonas* bacteremia shortly after transplantation. A patient on the waiting list who deteriorates to the point of requiring mechanical ventilation is kept active for transplantation as long as the patient can continue to undergo physical therapy. Tracheostomy was used to allow ventilated ambulation in two of the five patients on pretransplant mechanical ventilation. Eight other patients were hospitalized, close to requiring intubation, on up to 12 L per minute of oxygen therapy. The mean time on the waiting list for lung transplant recipients was 10 ± 2 months.

Donor lungs were evaluated with a chest x-ray, arterial blood gas on 100% fraction of inspired oxygen ($FiO_2$) and flexible bronchoscopy. In general, donors were acceptable if they were younger than 55 years of age with less than a 20-pack/year history of smoking. A chest x-ray clear of significant airspace disease with a partial pressure of oxygen ($PO_2$) greater than 300 mmHg on 100% $FiO_2$ was required. Bronchoscopy was used to document absence of persistent purulent secretions without evidence of aspiration characterized by significant edema and erythema of the airways. The donor lungs were flushed with 4 L of modified Euro-Collins solution preceded by infusion of 500 μg of prostaglandin $E_1$ before the aorta was cross-clamped.[11]

## Patient Characteristics: Heart–Lung Transplantation

Our approach to heart–lung transplantation is to perform the procedure only when lung transplantation with repair of a cardiac lesion (ventricular septal defect, atrial septal defect), which has resulted in Eisenmenger's syndrome, is not possible.[12] Patients with primary pulmonary hypertension, even those with severe right ventricular dysfunction, will do well after bilateral lung transplantation if the left ventricle is normal. The right ventricle shows significant and immediate improvement with normalization of afterload after lung replacement. We prefer to use the transverse "clam shell" incision via bilateral anterior thoracotomy to perform heart–lung replacement because of improved exposure of hilar structures and the posterior mediastinum, which can be the source of significant bleeding from systemic collateral vessels. The five patients undergoing heart–lung trans-

**Table 3. PRE-HEART TRANSPLANT MECHANICAL SUPPORT**

| Mechanical Support | No. |
|---|---|
| IABP | 25 (7–160 days) |
| LVAD | 5 (3–105 days) |
| ECMO | 1 (7 days) |

IABP = intra-aortic balloon pump; LVAD = left ventricular assist device; ECMO = extracorporeal membrane oxygenation.

**Table 4. LUNG TRANSPLANT RECIPIENT DIAGNOSIS**

| Diagnosis | No. |
|---|---|
| COPD | 24 |
| Cystic fibrosis | 10 |
| Primary pulmonary hypertension | 5 |
| Pulmonary fibrosis | 4 |
| $\alpha_1$-Antitrypsin deficiency | 4 |
| Eisenmenger's complex | 2 |
| LAM | 1 |
| Alveolar proteinosis | 1 |
| Sarcoidosis | 1 |

COPD = chronic obstructive pulmonary disease; LAM = lymphangioleiomyomatosis.

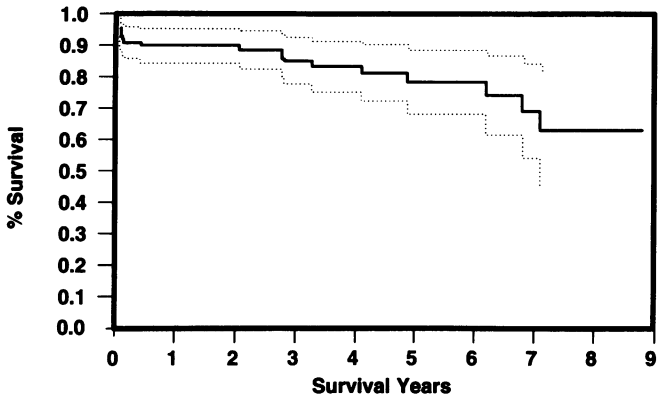


**Figure 2.** Kaplan-Meier survival estimate for cardiac transplant recipients.

plantation included two patients with Eisenmenger's syndrome with biventricular failure, one patient with complex congenital heart disease (pulmonary atresia with systemic collaterals to the lung, biventricular dysfunction), one patient with sarcoidosis involving both the heart and lungs, and one patient with cystic fibrosis with a severely deformed right main pulmonary artery and destroyed right lung.

## RESULTS

### Heart Transplant Recipients

The ischemic time for the 120 donor hearts was 148 ± 7 minutes, with a range of 55 to 250 minutes. In the majority of the patients, the Shumway atrioplasty technique was used for the atrial anastomosis. Later, patients were transplanted using bicaval anastomosis to optimize right ventricular filling and performance, and to reduce the incidence of bradyarrhythmias. Postoperative inotropic support was used to treat right ventricular donor dysfunction commonly seen in the first 24 to 48 hours postoperatively.[13] This usually consisted of low-dose epinephrine in combination with a phosphodiesterase inhibitor. In selected patients with persistent pulmonary hypertension and donor right ventricular dysfunction, inhaled nitric oxide at 40 to 80 ppm was used until extubation.[14]

There were ten postoperative deaths (8% operative mortality), with six due to allograft dysfunction, two from sepsis, one from postoperative pulmonary embolus, and one from bleeding and coagulopathy. Over a 5-year period from late 1990 to mid 1995, there were no operative deaths in 70 consecutive adult heart transplant recipients. The estimated survival of the group is illustrated in Figure 2, with a 1-year survival rate of 90% and a 5-year estimated survival rate of 80% (mean follow-up, 5 years).

The length of post-transplant hospital stay was 23.8 ± 4.0 days for the entire group. Since the implementation of a post-transplant care map, the length of stay for the last 25 patients has been reduced to 12.1 ± 2.4 days. All patients received at least one endomyocardial biopsy before discharge, and cyclosporine dosing was stabilized before release from the hospital.

Late mortality occurred in 11 patients from 1 to 7 years after transplantation. Infectious complications were responsible for three deaths, whereas two patients died of lymphoma. To date, only two patients have died of graft coronary artery disease. Hepatitis C, a ruptured aortic abdominal aneurysm, and a cerebrovascular accident accounted for one death each. One patient died of acute allograft rejection when he intentionally stopped taking cyclosporine 2 years after transplantation, in a successful suicide attempt.

Acute cellular rejection was assessed with surveillance endomyocardial biopsies performed monthly for the first 6 months then gradually decreasing in frequency to every 6 months by the third year after transplantation. The prevalence of acute cellular rejection was 25% at 30 days post-transplant and 75% at the end of 1 year. We have found a persistent, significant incidence of cellular rejection of 15% to 20% per year after 3 years post-transplantation, which has led to the policy of continuing regular surveillance biopsies late after cardiac transplantation. We have attempted to wean off prednisone by the third post-transplant year[15] and have been successful doing this in approximately 50% of the patients. Cyclosporine dosing also is reduced gradually so that by year 4, the targeted trough level is 100 ng/mL. If serum creatinine levels increase to more than 3 mg%, cyclosporine dosing is reduced, and prednisone is reinstituted or increased. Acute rejection episodes are treated with methylprednisolone (Solu-Medrol, Upjohn, Kalamazoo, MI) bolus therapy, with refractory rejection requiring rabbit antithymocyte globulin in a few patients.

Chronic allograft rejection in the form of graft coronary artery disease was assessed with coronary arteriograms performed at least every 2 years after transplantation. Stress thallium perfusion scans were performed on alternate years if the prior coronary arteriogram showed no disease. Of 50 patients studied with coronary arteriograms more than 3 years after transplantation, 5 had coronary lesions of greater than 25% in one or more vessels (10% incidence). Two of these patients died within 1 year of diagnosis (both 7 years post-transplantation). The other patients have shown no clinical or anatomic progression of graft coronary artery disease.

### Lung Transplant Recipients

Single-lung transplantation was performed through a standard posterolateral thoracotomy incision with a

**Table 5. USE OF CARDIOPULMONARY BYPASS IN LUNG TRANSPLANT PROCEDURES (N = 52)***

| Procedure | No. |
|---|---|
| Primary pulmonary hypertension | 3/5 |
| Eisenmenger's complex (VSD patch) | 2/2 |
| Pulmonary fibrosis | 2/4 |
| Cystic fibrosis | 4/10 |
| COPD | 2/28 |

* Thirteen of 52 patients required CPB.
VSD = ventricular septal defect; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass.

double lumen endotracheal tube. A telescopic bronchial anastomosis was used with 4-0 polydioxanone suture and a modified interrupted figure-of-eight suture on the cartilaginous portion of the bronchus. An omental wrap was not used. Significant bronchial anastomotic complications occurred in two recipients, necessitating placement of an endobronchial silastic stent at the bronchial anastomosis. Bilateral sequential transplants were performed through a bilateral anterior (clam shell) thoracotomy incision with division of the sternum. Four patients had lung transplantation through a previous thoracotomy, two each in the single and bilateral lung groups.

Cardiopulmonary bypass was available for all procedures and was used in 13 of 52 patients (25%). Cardiopulmonary bypass was used in both patients with Eisenmenger's syndrome receiving bilateral lung transplantation and three of five patients with primary pulmonary hypertension receiving bilateral lung transplantation. The remaining two patients with primary pulmonary hypertension were treated with inhaled nitric oxide during transplantation to maintain adequate oxygenation and hemodynamics until the first lung was replaced. Cardiopulmonary bypass was used in other critically ill patients who had significant pulmonary hypertension and extremely limited pulmonary reserve, and in one patient who had an *associated* coronary artery bypass graft × 1 to the right coronary artery at the time of right single-lung transplantation (Table 5).

The ischemic time of the donor lung in the single lung group was 3.5 hours, similar to the 3.6-hour ischemic time of the first lung in the bilateral lung group. The second lung in the bilateral lung group had a mean ischemic time of 5.5 hours.

Five patients died in the postoperative period, resulting in an operative mortality rate of 8%. Two patients died of adenoviral pneumonia, two patients died of bacterial sepsis, and one patient with severe pulmonary fibrosis died of graft dysfunction after bilateral lung transplantation with lungs from a 66-year-old donor. Despite support with extracorporeal membrane oxygenation, this last patient died before retransplantation.

The mean length of stay was 23.4 days, with patients discharged before the first surveillance transbronchial biopsy if they were doing well clinically. All patients were discharged to home without oxygen therapy and were entered into a 4-week program of pulmonary rehabilitation at an on-site location. Pulmonary mechanics showed significant improvement after transplantation, with $FEV_1$ increasing from 20% of that predicted to 60% of that predicted for patients with chronic obstructive lung disease.

Late deaths occurred in five patients, including bronchiolitis obliterans in two patients who showed significant deterioration in $FEV_1$ at 5 and 18 months post-transplantation, and biopsy confirmed bronchiolitis obliterans in each. One patient each died from cerebrovascular accident, acute rejection, and lung cancer originating in the native lung of a single-lung recipient. The estimated survival for the group of 52 lung transplant recipients is illustrated in Figure 3, with a mean follow-up of 1 year.

Significant post-transplant pulmonary infections occurred in almost half the patients, with cytomegalovirus pneumonitis occurring in ten patients. Because of the aggressive use of prophylactic ganciclovir and cytomegalovirus hyperimmune globulin in at-risk patients, no patients died of cytomegalovirus pneumonia. Bacterial pneumonia occurring early after transplantation occurred in eight patients, with *Pseudomonas* pneumonia developing in four patients and methicillin-resistant staphylococcal pneumonia developing in four patients. All were treated effectively with antibiotics except one patient who died of *Pseudomonas* pneumonia 3 weeks after single-lung transplantation. Adenoviral pneumonia developed in two patients in the postoperative period, and both died. Two late infections with cryptococcal

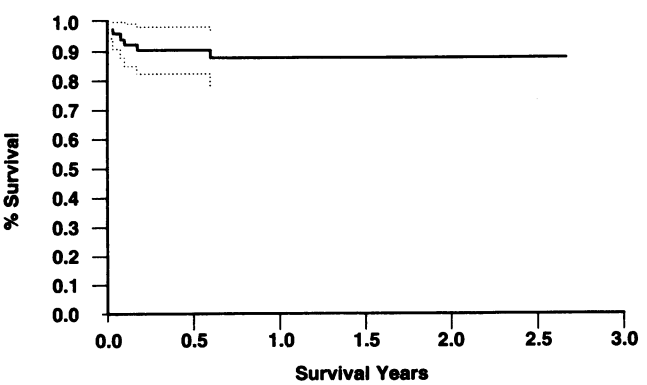


**Figure 3.** Kaplan-Meier survival estimate for pulmonary transplant recipients.

**Table 6. HEART–LUNG TRANSPLANT RECIPIENT CHARACTERISTICS**

| Patient Age (yr) | Patient Gender | Diagnosis | Outcome |
|---|---|---|---|
| 38 | Male | Cystic fibrosis | Died |
| 17 | Female | Eisenmenger's complex (redo) | Alive |
| 42 | Male | Eisenmenger's complex (redo) | Alive |
| 42 | Male | Sarcoidosis, cardiomyopathy | Died |
| 30 | Female | Congenital | Alive |

pneumonia occurred, one in association with cytomegalovirus. Both were treated with itraconazole.

Acute lung allograft rejection was diagnosed using clinical criteria in the early postoperative period (decrease in oxygenation, perihilar infiltrate on chest x-ray, drop in $FEV_1 > 10\%$, fever without evidence of organisms in bronchial specimens) and by using surveillance transbronchial biopsies in the late post-transplant period. Patients received three dally doses of Solu-Medrol 500 mg for grade 2 or greater rejections, according to the International Society for Heart and Lung Transplantation classification.[16] Acute cellular rejection documented by biopsy occurred in 31 of 52 patients (60%), with most of these episodes occurring within the first 3 months of transplantation during the first year. Half of those patients having histologic evidence of rejection had more than one episode of rejection confirmed by biopsy. Surveillance biopsies were performed every 3 months after transplantation, then every 6 months during the second year, and annually thereafter.

Chronic rejection in the form of bronchiolitis obliterans was confirmed histologically in two patients at 5 and 18 months post-transplantation. Each was a bilateral recipient, one with chronic obstructive pulmonary disease and the other patient with cystic fibrosis. The progressive unrelenting course, characteristic of the syndrome, was unaltered by augmentation of immunosuppression.[17]

### Heart–Lung Recipients

Clinical application of heart–lung transplantation remains at a low level because conditions previously treated with heart–lung transplantation (primary pulmonary hypertension, cystic fibrosis, Eisenmenger's syndrome with intact left ventricular function) currently can be treated effectively with lung transplantation. Furthermore, the allocation algorithm used by most organ procurement agencies is designed inherently so that a heart–lung block from a single donor will be divided to more than one recipient. The clinical outcome of five patients undergoing heart–lung transplantation is shown in Table 6. Severe, uncontrollable coagulopathy and bleeding developed in the first patient before the availability of aprotinin. With the use of aprotinin, two subsequent patients who had undergone prior ventricular septal defect closure with persistent pulmonary vascular obstructive disease and biventricular failure underwent successful heart–lung transplantation. The second death in this small population occurred in a patient with severe sarcoidosis involving both lungs and the heart. This patient had an aspergilloma in the native right lung. He was treated with amphotericin B post-transplantation, but still died 3 weeks postoperatively of systemic aspergillosis.

## DISCUSSION

This review of a single center's thoracic transplantation program documents that heart and lung replacement in morbidly ill patients can be performed with less than a 10% operative mortality. In our small series of heart–lung transplantation, the operative mortality was much higher (40%), partially related to suboptimal patient selection early in our experience with this procedure. The 5-year survival rate of 80% of our heart transplant recipients compares favorably with the 70% 5-year survival rate in UNOS-compiled statistics. The limited follow-up in our lung transplant recipients precludes estimate of a 5-year survival, but from other centers' experience with longer follow-up, it appears that a 50% survival rate at 5 years can be expected after lung transplantation.[4]

Because of the large number of patients with ischemic cardiomyopathy referred for cardiac transplantation and the limited number of cardiac donors, which has not increased over the past several years, we systematically have evaluated all patients referred for transplantation with ischemic cardiomyopathy for coronary artery bypass grafting using a careful preoperative assessment.[18,19] Using positron emission tomography scanning to determine myocardial viability and right heart catheterization to assess the degree of physiologic decompensation resulting from a low ejection fraction, high-risk coronary artery bypass graft can be performed in selected patients with an operative mortality of approximately 10%. A comparison of long-term survival of patients undergoing cardiac transplantation at Duke with a group of patients undergoing surgical revascularization for ischemic cardiomyopathy is illustrated in Figure 4. Over a 10-year period, 118 patients with an ejection fraction less than 25% (mean 21%), underwent coronary artery bypass graft.[20] This group had a high (68%) incidence of class III or class IV congestive heart failure and was older than the transplant group. The survival curves quickly separate, and at 5 years postoperatively, the survival in the coronary artery bypass graft group (60%) is significantly

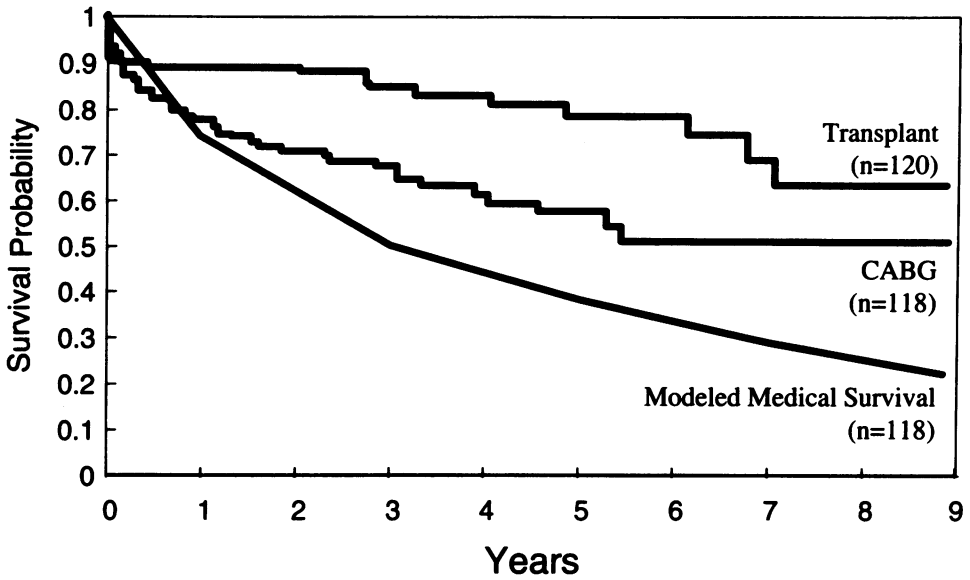


**Figure 4.** Estimated survival (Kaplan-Meier) for 118 patients with ischemic cardiomyopathy treated with coronary artery bypass graft compared with the cardiac transplant group. Also shown is the model estimated survival for medical therapy alone.

lower than the survival in the transplant group (80%). However, if a pretransplant waiting list mortality rate of 20% is taken into consideration, the overall efficacy of each treatment probably would approach the same survival estimate. Also shown is a model for estimated survival with medical therapy alone using the Cox proportional hazards method from a matched cohort of patients with ischemic cardiomyopathy treated medically for coronary artery disease at Duke. The 38% 5-year survival in this group falls well below either surgical group.

After surviving the wait for a donor organ, the most serious risk to long-term survival faced by a heart or lung transplant recipient is chronic rejection. In cardiac recipients, this is manifested by graft coronary artery disease. Although an immune mechanism is postulated in the etiology of this disease, mechanisms known to be involved in atherosclerosis in nontransplant patients probably are also involved.[21] The relatively low incidence of graft coronary artery disease in this series (10%) compared with an often cited incidence of more than 30% at 3 years post-transplantation is not explained clearly. We have maintained routine surveillance biopsies in an attempt to reduce the contribution of rejection to this disease, as well as careful follow-up and aggressive treatment of elevated lipids. We do not have intracoronary ultrasound images to quantitate intimal thickening, which might be predictive of subsequent stenoses and death from graft coronary artery disease.[22]

Bronchiolitis obliterans syndrome is the major cause of late morbidity and mortality in lung transplant recipients.[23] The prevalence of this progressive and debilitating disease is approximately 40%, usually developing between 15 to 30 months after lung transplantation. It represents a chronic immune response directed against the lung allograft. Bronchiolitis obliterans syndrome appears to affect all subgroups of lung transplant recipients without distinction for age, sex, type of transplant, or underlying diagnosis. Because of its proposed immunologic mechanism, most centers treat this with augmented immunosuppression, but this usually is with minimal benefit. We have used an induction course of rabbit antithymocyte globulin for 3 days post-transplantation in a randomized prospective trial to determine its potential efficacy in reducing the long-term incidence of bronchiolitis obliterans syndrome.

## CONCLUSION

Early and intermediate survival for heart, lung, and heart–lung transplantation for one center is reviewed using current techniques of organ procurement, pre- and postoperative support, and cyclosporine-based immunosuppression. Despite directing thoracic organ replacement to critically ill patients, some requiring mechanical circulatory or ventilatory support, early survival is 80% to 90% at 1 year. The greatest risk to long-term survival in these patients is chronic allograft rejection and dysfunction.

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## Discussion

DR. JAMES D. HARDY (Jackson, Mississippi): Dr. Van Trigt's results with his colleagues at Duke are superb; I congratulate them. May I have the movie, please?

This movie presents the first lung transplant in man and the first heart transplant in man. This is the insertion of the first lung transplant more than 30 years ago. We have anastomosed the superior pulmonary vein, the inferior pulmonary vein, and the pulmonary artery and now we will complete anastomosing the bronchus.

This man had a carcinoma of the left lung which had blocked the main stem bronchus, and had spread to his chest wall as well. We are shown here taking blood samples to identify and document the fact that this lung that has just been inserted is performing respiration effectively and it was.

Now I am going to stop the movie showing the first heart transplant in man and show the first of two slides.

As seen, the first lung transplant was published in 1963 (*JAMA 186*).

Next slide, please.

This is the heart transplant we performed in 1964 (*JAMA 188*). And, Mr. Moderator, may I introduce three people? All right. I want to ask these three people to stand. The first is Dr. Carlos Chavez. Carlos, welcome. The next is Dr. Martin Dalton. And the third is Dr. George Walker. Dr. Chavez collaborated on the first heart transplant, and Drs. Dalton and Walker assisted with the first lung transplant.

Thank you very much.

DR. PETER VAN TRIGT (Closing Discussion): I think I 'd like to express my gratitude to Dr. Hardy for sharing those historic moments with us again. It is because of his pioneering surgical work thirty years ago in combination with the advances in immunosuppression and advances in treating infectious disease that has allowed us to achieve the survival benefits that we are able to do today. Thank you very much, sir.